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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.          | CONFIRMATION NO. |
|-----------------|-------------|----------------------|------------------------------|------------------|
| 09/818,066      | 03/27/2001  | Shuping Tong         | 00786-287004 /<br>MGH-0960.3 | 1622             |

26161 7590 02/25/2003

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EXAMINER

LUCAS, ZACHARIAH

|          |              |
|----------|--------------|
| ART UNIT | PAPER NUMBER |
|----------|--------------|

1648

DATE MAILED: 02/25/2003

12

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/818,066

Applicant(s)

TONG ET AL.

Examiner

Zachariah Lucas

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 27 November 2002.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

## DETAILED ACTION

### *Status of the Claims*

1. Claims 1-9 are pending and under consideration in this application. The claims were rejected in the action ailed on May 21, 2002 (the prior action), and were amended in the response filed November 27, 2002 (Amend. B).
2. The Art Unit location of your application, and the examiner to whom the case has been docketed in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Zachariah Lucas in Art Unit 1648.

### *Specification*

3. **(Prior Objection-Maintained)** The use of trademarks in the application was noted in the prior action. It was further noted that, when used in an application, the trademarks should be capitalized wherever it appears *and be accompanied by the generic terminology*. No such generic description has been provided for the AMPLIFY™ solution. See e.g., page 19, lines 10-13.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

### *Claim Objections*

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4. **(New Objection-Necessitated by Amendment)** Claim 9 is objected to because of the following informalities: the word "the" should be inserted between the words "wherein" and "polypeptide" in line 1 of the claim. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. **(Prior Rejection- Withdrawn)** Claim 1 and 6 were rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The examiner finds the applicant's argument persuasive, and the rejection is hereby withdrawn. It is clear that the claim as written reads on hepatitis virus pre-S proteins, or fragments thereof, other than those disclosed in the application.

7. **(Prior Rejection-Withdrawn)** Claims 5 and 9 were rejected in the prior action under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The examiner finds the applicant's arguments persuasive. The rejection is therefore withdrawn.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. **(Prior Rejection- Maintained)** Claims 1-9 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The applicant's traversed this rejection on the basis that they disclosed 29 species of hepadnavirus pre-S polypeptides, and that there is little variability among them. The examiner does not challenge that the applicant has disclosed multiple varieties of the pre-S protein. However, as the examiner stated in the prior action, the applicant has disclosed only two species of the claimed genus.

The claimed genus is not simply a collection of hepadnavirus pre-S peptides, but the combination of such into a polypeptide comprising residues 1-104 or a pre-S protein, or a fragment thereof with at least residues 80-102, and "one or more amino acid sequences that are not identical to any part of the pre-S protein." Thus, the fact that the applicant has disclosed numerous hepadnavirus pre-S proteins does not alone provide written description support for the claimed inventions. In this case, written description support requires that there be examples not only of the pre-S proteins, but also of combinations of such with other non-pre-S proteins into the claimed polypeptides. The "substantial variability" among the species arises in part because the fusion protein may include not only the pre-S fragments but also any other protein or protein fragment.<sup>1</sup> The applicant has shown only two species of this genus, both of which are a combination of a pre-S peptide with a glutathione S-transferase (GST). The applicant has not shown any combination of a pre-S protein with any other peptides. Further, it does not appear

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<sup>1</sup> With regards to applicant's request for support for the examiner's contention that there is "substantial variability among the species," it is noted that the hepadnavirus fragments claimed are not limited to those in Figures 16 and 17. Substantial variability in the claimed fragments can be seen for example between residues 80-102 of SEQ ID NOs: 34 and 45. In this range of residues- a fragment claimed in claim 1, these two sequences do not share a single residue unless aligned as per Figure 20. Thus, they vary substantially from each other.

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that the specification either teaches or suggests that the claimed pre-S fragments may be fused with any other protein than the full length GST. See, e.g. pages 7, 17, 50 (all describing fusion proteins of the Pre-S fragments and GST). Thus, the applicant has not provided sufficient written description support for the full breadth of the present claims. There is no support of a polypeptide comprising the claimed pre-S fragment with any amino acid sequence other than the GST protein. The rejection is therefore maintained for the reasons above and for the reasons of record.

10. **(Prior Rejection-Withdrawn)** Claims 1-9 were rejected in the prior action under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polypeptides consisting of aa sequences corresponding to the aa sequence do the HBV or DHBV pre-S proteins with glutathione S-transferase which are disclosed in the specification, does not reasonably provide enablement for polypeptides consisting of aa sequences corresponding to all other naturally occurring hepadnaviruses with any heterologous sequence.

The applicant traverses this rejection on the grounds that the applicant has provided "detailed teachings" regarding the claimed invention, including the disclosure of other strains of HBV. In particular, the applicant argues that critical fragments and amino acids of new sequences may be identified by comparing such sequences to those disclosed in the application. In particular, the applicant points to Figure 20 of the application which shows a different set of rules for determining important fragments in the disclosed sequences. The examiner agrees that it appears that the critical fragments may be identified using the marked residues identified in Figure 20. It is also noted that Arginine 99, the residue identified as essential for hepadnavirus infection (binding) of a host cell, or a residue corresponding thereto according to the sequence comparison demonstrated in figure 20, appears to fall within the region of residues 80-102 in all

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of the disclosed pre-S proteins despite variations in the protein sequences. In view of this, the rejection is withdrawn.

***Claim Rejections - 35 USC § 103***

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

12. **(Prior Rejection-Withdrawn)** Claims 1 and 6 were rejected under 35 U.S.C. 103(a) as being unpatentable over Cabezon et al. (EPA 0278940). These claims describe a polypeptide consisting of a first amino acid sequence identical to 1) amino acids 1-104 of a naturally occurring hepadnavirus pre-S protein or 2) a fragment of that sequence including at least amino acids 80-102 if the pre-S protein, and one or more heterologous amino acids not identical to any part of the pre-S protein. The applicant traversed this rejection arguing that Cabezon does not teach that or suggest the use of any pre-S sequence other than the full length of the protein. More particularly, the applicant argues that the reference does not teach or suggest the fragments claimed in the present application.

The examiner finds the applicants arguments persuasive. Because the claims do not read on the full length pre-S protein, and because Cabezon neither teaches nor suggests the use of any fragments of the pre-S protein, much less the fragments identified by the applicant, the rejection is hereby withdrawn.

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13. **(Prior Rejection-Withdrawn)** Claims 5 and 9 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Cabezon in view of Khudyakov et al, (J. Virol., 68(11): 7067-7074). Applicant traverses this rejection for substantially the same reasons as the above with regards to the Cabezon reference alone. Applicant adds only that Khudyakov does not teach the elements missing from Cabezon. The Examiner finds the applicant's arguments persuasive. The rejection is therefore withdrawn.

### *Conclusion*

14. No claims are allowed.

15. The following prior art reference is made of record and considered pertinent to applicant's disclosure. However, while relevant it is not used as a basis for rejection for the stated reasons.

U.S. Patent 5,204,096, issued to Neurath et al. Claims 2, 5, and 9 describe a hepatitis vaccine comprising a sequence of at least 26 amino acids from the pre-S protein regions of residues 1-120. This is relevant as such fragments include fragments comprising at least residues 80-102. However, the reference does not teach or suggest the particular fragments described in the present claims.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

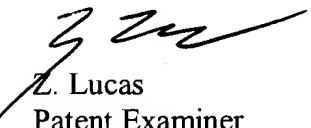
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the




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organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

  
Z. Lucas  
Patent Examiner  
February 18, 2003

  
JAMES HOUSEL 2/23/03  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600